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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,924	08/18/2006	Franz Xaver Schwarz	16525-33660	1065

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EXAMINER	
AHMED, HASAN SYED	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
11/09/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,924	SCHWARZ, FRANZ XAVER	
	Examiner	Art Unit	
	HASAN AHMED	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's appeal brief, filed on 1 August 2011. After further consideration, in view of the remarks presented in the appeal brief, the finality of the previous Office action is withdrawn. The following are new grounds of rejection, except the 35 USC 112, 1st paragraph rejection over claim 48, which has been maintained.

* * * * *

Status of the Claims

Claims 36-58 are treated on the merits in this action. No claims have been amended, cancelled, withdrawn, or allowed. The following rejections are newly applied except the 35 USC 112, 1st paragraph rejection over claim 48, which has been maintained. They constitute the complete set presently being applied to the instant application.

* * * * *

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, claim 48 claims the process of claim 36 wherein the granulate is free of pharmaceutically acceptable excipients. Examiner respectfully submits that this claim contradicts the claim from which it depends, i.e., claim 36, because claim 36 recites a granulate comprising micronized amoxicillin trihidrate and sugar. Sugar is routinely used in the pharmaceutical art as a pharmaceutically acceptable excipient (e.g., an inert core, a binder, or a filler). As such, the specification does not reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 36, 38, 39, 41-46, 50, 51, 53, and 54-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 080 862 (“Grimmett”) (cited in the IDS filed on 18 August 2006) in view of WO 03/063820 (“Schwarz”) (cited in the IDS filed on 18 August 2006), further in view of U.S. Patent No. 4,177,254 (“Khan”) (cited in the IDS filed on 18 August 2006), as evidenced by U.S. Patent No. 7,157,094 (“Gaytan”) (currently of-record), as further evidenced by merriam-webster.com (definition of "wet").

Grimmett discloses water-dispersible extruded granules comprising amoxicillin trihydrate and sugar (see e.g. page 1, line 14; claim 1). The granules are prepared by, "…bringing into association the components [of the granule] and thereafter extruding the blended mixture." See page 3, lines 2-6. The amoxicillin trihydrate and sugar, *inter alia*, are passed through a screen (reading on claim 36) (see example 1).

Disclosed granulation solvents include hygroscopic hydrophilic organic solvents such as methanol, ethanol, n- and iso-propanol (see page 2, lines 25-26). While Grimmett does not explicitly teach the use of water in the granulation liquid, Grimmett teaches that formulation of the disclosed composition can take place in an atmosphere of up to 40% relative humidity (see page 3, line 9).

It should be noted that Grimmet does not prohibit the use of water or teach against the addition of water to the granulation liquid. To the contrary, the Grimmett disclosure implicitly suggests that some level of water content exists in the granulate and granulation liquid, based on the following teachings:

(a) Grimmet does not state anywhere that water should not be present in the granulation liquid, or that the presence of water in the granulation liquid will have adverse consequences for the final product;

(b) In an atmosphere of up to 40% relative humidity, hygroscopic hydrophilic organic solvents such as methanol, ethanol, n- and iso-propanol will inherently absorb water from the environment. It is noted that since claim 36 does not include a lower limit water concentration, one molecule of water in the granulation liquid reads on claims 36 and 58 as currently constructed;

(c) Grimmett teaches a 35 minute drying step after extrusion at a temperature of up to 45 degrees C (113 degrees F) (see, e.g., Example 1). Such an extensive drying step would only be required if Grimmett's extruded mass were wet with some level of water content; i.e., if the granulate contained only volatile organic solvents with absolutely no water, such extensive drying step would not be required or disclosed;

(d) Applicants recite the limitation "wet extruded mass" in claims 36 and 55, however the term "wet" has a broad scope of meaning, including a *de minimis* amount of moisture (see, e.g., Merriam-Webster definition of "wet", including: (1)(a) consisting of, containing, covered with, or soaked with a liquid (as water); or (6) employing or done by means of or in the presence of water or other liquid). The instant specification provides no guidance as to how much moisture is required for the extruded mass to fall within the scope of a "wet" extruded mass. Grimmett states that tightly bound water normally has little adverse effect on stability (see page 2, lines12-14), suggesting the excipients may be covered with or contain an amount of water and that the extrusion may occur in the presence of water, meeting the definition of "wet" recited in the Merriam-Webster dictionary and meeting the scope of the instant claims with respect to the amount of water required to meet the claims; and

(e) Applicant states in the appeal brief (filed on 1 August 2011) that "[c]laim 36 specifically recites "extruding the sieved mixture with a granulation liquid comprising water to obtain a wet extruded mass," which clearly requires the active process step of adding far more than a single molecule of water to form the wet extruded mass." See appeal brief, page 8, second full-paragraph. Thus, applicant reasons that the limitation

"wet extruded mass" suggests that the mass contains far more than a single molecule of water. Similarly Grimmett, while not explicitly reciting the use of water in the granulation liquid, explicitly describes the mass resulting from the granulation step as a "wet mass" (see examples 3 and 6). Based on applicant's own reasoning, Grimmett's description of the mass as a "wet mass" suggests that Grimmett's extruded product contains "far more than a single molecule of water", which presumably is present (as stated above) because of absorption of ambient water by the hygroscopic hydrophilic organic solvents being used.

Again, examiner respectfully notes that no minimum amount of water in the granulation liquid is being claimed and no minimum amount of water in the granulation liquid is disclosed in the specification; as such, the amount of water inherently present in Grimmett's granulation liquid, even if the amount is *de minimis*, meets the scope of the claims as they are currently constructed. Importantly, Grimmett does not state anywhere that the disclosed granulation liquid should not contain any water; to the contrary, as outlined above, Grimmett suggests that the disclosed granulation liquid contains some amount of water.

In any event, Schwarz teaches granulation of a beta-lactam antibiotic wherein the granulation liquid may be water, or an organic solvent, or an organic solvent mixed with water, preferably water or an organic solvent mixed with water (see page 5, lines 6-19). The beta-lactam antibiotic may be used in dry form (see page 5, lines 7 and 13). Disclosed organic solvents include alcohols, such as ethanol (see page 5, line 17) (also disclosed by Grimmett, see page 2, line 25). The granulation mass is then extruded

(see page 5, line 28) and sieved (see page 5, line 33). Disclosed beta-lactam antibiotics include amoxicillin trihydrate (see page 3, lines 9-10). The resultant granulate provide a directly usable pharmaceutical composition (see page 12, lines 21-23), suggesting that use of water in the granulation liquid results in stable beta-lactam antibiotic containing granulates. Disclosed compositions include a suspension granulate which may be reconstituted in an appropriate liquid, to provide a pharmaceutical oral suspension (see page 13, lines 4-6).

Khan teaches the preparation of amoxicillin trihydrate granules prepared by fluid bed granulation using sucrose as a binder (see, e.g., abstract). Disclosed binders include non-hygroscopic binders such as those disclosed by Grimmett (e.g. hydroxypropylcellulose – see col. 2, line 53). Regarding the granulation liquid (the solvent in which the binder is dissolved), Khan teaches that, "[t]he solvent used to dissolve the binder may be any pharmaceutically acceptable inert solvent for the binder which is sufficiently volatile to be readily removed from the particles in the drying step. Examples of such solvents include water, methanol, ethanol, n- and iso-propanol, chloroform, methylene chloride, acetone, methylethylketone, methyl acetate, ethyl acetate, trichloroethylene, tetrachloroethylene, carbon tetrachloride, or like solvents or homogeneous mixtures of such solvents. Water is normally the solvent of choice due to its ready availability, and because organic solvents have to be carefully collected when vaporized in the drying step." See col. 4, lines 35-47; emphasis supplied. Additionally, Khan states that the disclosed granules have excellent stability properties (see col. 1, line 30).

The extruded product of Grimmet is collected and passed through a screen and dried (reading on claim 36) (see example 1). The dried extrudate is then blended with 5% SYLOID (reading on the homogenization of claim 36) (see example 1). The granulate may be dissolved in water to form a syrup (reading on the smooth suspension of claim 36) (see page 3, lines 18-19). Sugar is the common word for sucrose, as such, the sugar disclosed by Grimmett is deemed to be functionally equivalent to the sucrose of instant claims 38, 39, and 44. Amoxycillin trihydrate concentration is disclosed as, e.g., 13.65% (reading on the ranges recited in instant claims 41-43) (see example 1). Sugar (sucrose) concentration is disclosed as, e.g., 68.9% (reading on the concentration recited in claim 44) (see example 1). The granulate particle size is disclosed as 1000 micrometers (reading on claims 45, 46, 53, and 54) (see example 1). The process disclosed by Grimmett does not involve grinding or micronizing (reading on claim 50).

Regarding claim 51, Grimmett discloses an extrusion step (see above). While Grimmett does not disclose an extrusion temperature, it is known in the art that temperatures in extruders operating at normal, commercial extrusion rates expose extruded material to temperatures of 25 to 100 degrees C (see Gaytan, col. 1, lines 38-40).

Grimmett differs from the instant application in that it does not teach the particle sizes recited in claims 55-57. As indicated above, Schwarz teaches granulation of a beta-lactam antibiotic wherein the granulation liquid may be an organic solvent mixed with water (see page 5, lines 6-19). The granulation mass is then extruded (see page 5,

line 28) and sieved (see page 5, line 33). Disclosed beta-lactam antibiotics include amoxicillin trihydrate (see page 3, lines 9-10). One disclosed average grain size is 30 micrometers (see page 10, line 20), reading on the particle size ranges recited in claims 55-57. Schwarz explains that the disclosed particle size is beneficial for the production of a granulate that is stable to segregation (see page 10, line 19).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to prepare a stable granulate for reconstitution with water into an oral aqueous suspension comprising micronized amoxicillin trihydrate and sugar, the process comprising screening a mixture of amoxicillin trihydrate and sugar through a first sieve, extruding the sieved mixture with a granulation liquid comprising water to obtain a wet extruded mass; screening the wet extruded mass through a second sieve to provide a sieved wet extruded mass; drying the sieved wet extruded mass, and homogenizing the dried sieved extruded mass to obtain a granulate comprising micronized particles of amoxicillin, as taught by Grimmett in view of Schwarz, further in view of Khan, as evidenced by Gaytan. One of ordinary skill in the art at the time the invention was made would have been motivated to use said process because it results in a composition comprising amoxicillin trihydrate in the form of an extrudate suitable for direct ingestion or dispersion in water prior to ingestion, as explained by Grimmett (see page 2, lines 11-14). Additionally, one of ordinary skill in the art at the time the invention was made would have been motivated to use a granulation liquid comprising water because it is readily available, produces a class of granules having excellent stability properties, and because organic solvents have to be carefully collected when

vaporized in the drying step, as explained by Khan (see above). Finally, one of ordinary skill in the art at the time the invention was made would have been motivated to use a granulate comprising particles of amoxicillin sized between 0.1 and 100 micrometers because it produces a granulate that is stable to segregation, as explained by Schwartz (see above).

*

2. Claim 37 rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 080 862 ("Grimmett") (see above) in view of WO 03/063820 ("Schwarz") (see above) further in view of U.S. Patent No. 4,177,254 ("Khan") (see above) in view of U.S. Patent No. 6,242,382 ("Bratz") (currently of-record).

Grimmett, Schwartz, and Khan are discussed above. Grimmett differs from the instant application in that it does not teach a granulation liquid comprising sugar. However, use of a granulation liquid comprising sugars in extruder granulation techniques was known in the art at the time the instant application was filed as evinced by Bratz (see col. 14, lines 30-31). Bratz discloses sugars as binders in the granulation liquid (see col. 14, line 28). Khan explains that use of binders such as sucrose in a granulation liquid is beneficial because reconstitution of granules made with binders such as sucrose readily yields a suspension of the active ingredient (see col. 2, lines 48-57).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use sugar in a granulation liquid, as taught by Grimmett in view Schwartz, further in view of Khan, further in view of Bratz. One of ordinary skill in the art

at the time the invention was made would have been motivated to use a sugar in a granulation liquid because reconstitution of granules made with binders such as sucrose readily yields a suspension of the active ingredient, as explained by Khan (see above).

*

3. Claims 40 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 080 862 ("Grimmett") (see above) in view of WO 03/063820 ("Schwarz") (see above) further in view of U.S. Patent No. 4,177,254 ("Khan") (see above) in view of U.S. 2002/0006433 ("Davidson") (cited in the IDS filed on 18 August 2006).

Grimmett, Schwartz, and Khan are discussed above. Grimmett explains that the disclosed composition is beneficial the treatment of bacterial infections (see page 1, line 3). Grimmett differs from the instant application in that it does not teach the sugar alcohol of instant claim 40 or the homogenization conducted in a tumbler mixer of instant claim 52. Regarding claim 40, granulate compositions comprising amoxicillin trihydrate and mannitol were known in the art at the time the instant application was filed, as evinced by Davidson (see, e.g., p. [0021]). Davidson explains that mannitol is beneficial as a chewable base (see, e.g., p. [0006]).

Regarding claim 52, the process of blending the dried extrudate with 5% SYLOID is deemed to be functionally equivalent to the homogenization conducted in a tumbler mixer, since both processes will result in mixing of a sieved extrudate, which in turn will result in homogenization of the dried, sieved, extruded mass.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose a method of making a granulate comprising amoxicillin

trihydrate and mannitol, as taught by Grimmett in view of Davidson. One of ordinary skill in the art at the time the invention was made would have been motivated to use mannitol because it is beneficial as a chewable base, as explained by Davidson (see above).

* * * * *

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7-12, 17, and 18 of copending Application No. 11/813,380 ('380). Although the conflicting claims are not identical, they are not patentably distinct from each other because '380 claims a process for preparing a stable granulate comprising amoxicillin trihydrate, the process

comprising: (a) extruding a mixture comprising amoxicillin trihydrate in an aqueous mixture, (b) granulating the moist extruded mass through a sieve, and drying the granulate (see claim 1). '380 differs from the instant application in that it does not explicitly claim a screening step prior to extrusion or a homogenizing step after drying, however these steps were known in the art, as shown by Grimmett (see above).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

Response to Arguments

Applicant's arguments with respect to the 35 USC 112, 1st paragraph rejection over claim 48 in the appeal brief filed on 1 August 2011 has been fully considered but is not persuasive. Applicant argues that the originally filed specification distinguishes between the required "sugar" and "pharmaceutically acceptable excipients" in that sugar is not listed in the examples of "pharmaceutically acceptable excipients" disclosed in page 5, first paragraph (see appeal brief, pages 5-6). Examiner respectfully submits that this argument is not persuasive because the list cited on page 5 of the specification is not all-inclusive; i.e., it uses the phrase, "for example". Additionally, the specification does not explicitly or implicitly state that "sugar" is not an excipient. As indicated in the substantive rejection, sugar is routinely used as an excipient in the pharmaceutical arts. Inclusion or exclusion from a list is not a definitive and exclusive definition. This rejection could be overcome by amendment to recite the absence of any excipient other than sugar.

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Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HASAN AHMED whose telephone number is (571)272-4792. The examiner can normally be reached on 9am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571)272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/H. S. A./
Examiner, Art Unit 1615

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